

### **REMARKS/ARGUMENTS**

Claims 1-9 are pending in the instant application. Claims 1-4, 8, and 9 stand rejected under 35 U.S.C. §103(a) as being unpatentable over United States Patent No. 5,132,309 in view of DE 29609958 to Schott Glaswerke or United States Patent No. 6,200,658 to Walther. Claims 1, 5, 6, 8, and 9 stand rejected under 35 U.S.C. §103(a) as being unpatentable over United States Patent No. 5,545,396 to Albert et al. in view of either Schott Glaswerke or Walther. Claims 1, 5, and 7-9 stand rejected under 35 U.S.C. §103(a) as being unpatentable over United States Patent No. 6,466,814 to Ardenkjaer-Larsen in view of either Schott Glaswerke or Walther. Reconsideration is respectfully requested.

**1. Claim Rejections : 35 USC § 103(a): Claims 1-4, 8 and 9**

Claims 1-4 are 8 and 9 stand rejected as obvious over the combination of Felder (US 5132409) with either one of Schott DE 29609958 or Walther (US 6200658). This rejection is respectfully traversed.

The Examiner states that:

**“It would have been obvious to one of ordinary skill in the art to modify the compositions disclosed by Felder (i.e., non-radioactive metal complex diagnostic agents) by using vials having a silica coated [sic] inside because it is known in the art that such vials provide various advantages for the storage of pharmaceuticals, specifically including diagnostic agents, as taught by, DE’958 and Walther, as stated above. One of ordinary skill in the art would have been motivated to use such improved silica coated vials for the pharmaceutical compositions disclosed by Felder to take advantage of one or all of the advantages taught in the prior art in using such vials for pharmaceuticals, as stated above.”**

The Examiner reasons that the person skilled in the art would be motivated to apply any and all improvements which are said to be useful for a given product in the same field. Applicants respectfully submit that, in reality, the person skilled in the art would inevitably need to exercise judgement as to which specific elements of any prior teaching should be chosen to be improved.

The Examiner alleges that Felder discloses that the non-radioactive metal complex contrast agent compositions are contained in vials. Applicants can find no such general teaching in Felder. The only disclosure of vials in Felder seems to be in Examples 14-19, which relate to gadolinium complexes of specific macrocyclic chelators. Columns 1-8, Examples 1-13 and the claims of Felder are thus silent on this aspect. Applicants also point out that Felder discloses new macrocyclic chelating agents which have a "wide range of applications" (Column 2 lines 18-30). These include several applications which do not relate to medical diagnostic imaging such as "recovery, separation, selective extraction of metal ions even at very low concentrations" and therapeutic uses as detoxification agents (Column 2 lines 20-24).

Felder's general silence on vials shows that vials are not regarded by Felder as a significant part of the invention. Indeed, given the "wide range of applications" contemplated by Felder, many would presumably not even be suitable for use in vials. Applicants therefore contend that the person skilled in the art would be unlikely to select to improve this element of Felder, which is mentioned only in selected Examples and is given no weight by Felder.

Applicants also contend that the person skilled in the art, even if assumed to be contemplating improvement of Felder, would focus on the teachings in Felder of what is important, and be motivated to improve those elements. In Felder these are clearly the design of the chelating agent, which is described at length at Column 5 line 25 to Column 7 line 65.

Such improvements all teach away from the present invention. Applicants therefore contend that there is no motivation to change Felder in the specific manner suggested by the Examiner without the application of hindsight, ie. reference to the present invention.

Further comments on the specific document combinations cited by the Examiner are given below:

**1.1 Felder and DE 29609958.**

DE'958 teaches that glass containers having an inner surface coating of oxides or nitrides of silicon, titanium, tantalum and/or aluminium are useful to reduce leaching of impurities from the glass walls into the contents. There is no teaching or suggestion in Felder that the compositions therein suffer from such leaching problems. Indeed, as noted above, Felder hardly even mentions vials. Hence, applicants contend that there would be no motivation for the person skilled in the art to modify Felder in the manner suggested by the Examiner.

Also, DE'958 teaches that a very wide range of oxide or nitride coating materials can be used. The combination of Felder with DE '958 would therefore logically also give a wide range of possibilities – and would provide no motivation to select only the specific teaching of the present claims. Silica is said by DE'958 to be preferred, but the only “diagnostic solution” taught by DE'958 is blood and blood samples. DE'958 provides only limited information, so no further description is supplied. As the person skilled in the art would be unlikely to use DE'958 as a source of teaching on diagnostic agents which are not based on biological fluids or proteins such as blood, Applicants respectfully submit that the the suggested combination of references fails to disclose, teach, or suggest the present invention. Withdrawal of the rejection is respectfully requested.

**1.2 Felder and Walther.**

The Examiner refers to Column 2 of Walther (US 6200658). Applicants presume that lines 49 to 57 is the section referred to:

**“In order to avoid the disadvantages of dealkalizing process it is also known to provide a tubular glass container from low melting glass material, which operates as a packaging device for pharmaceutical materials, having a silicon dioxide (SiO<sub>2</sub>) layer on its interior surface, which has the same inertness as a quartz glass surface (M. Walther, "Packaging of sensitive parenteral drugs in glass containers with a quartz-like surface", in Pharmaceutical Technology Europe, May, 1996, Vol. 8, Nr. 5, pp. 22 to 27.”**

Applicants submit that Walther is in fact silent on vials, Walther refers to ‘hollow glass bodies’. These are described at Column 1 lines 27-41. The Examiner’s attention is drawn to Column 1 lines 20 to 41, where ampoules, bottles, etc are mentioned but not vials. The section of text that the Examiner relies on at Column 2 is in fact unrepresentative of Walther. Thus Walther itself does not limit the nature of the “oxide material” used in the coatings to silica. Even at Column 4 lines 40 to 43, Walther teaches that:

“... the following oxides may be used, among others, as coating materials: SiO<sub>2</sub>, Al<sub>2</sub>O<sub>3</sub>, TiO<sub>2</sub> or mixtures thereof”.

Applicants therefore contend that Walther provides no clear teaching that silica is to be used. The combination Felder and Walther in fact leads to a range of possibilities, not fails to disclose, teach, or suggest the specific teachings of the present claims. As the combination of Felder and Walther provides no motivation to combine the references in a manner so as to render the present invention obvious, Applicants

therefore contend that the obviousness objection based on this combination should be withdrawn.

The Examiner's comments with respect to PCVD (Claim 8) are believed moot, since Claim 8 depends on Claim 1, and the above demonstrates that Claim 1 is non-obvious over the prior art of record.

Therefore, as neither DE'958 nor Walther, either alone or in combination, correct the deficiencies of Felder in a manner as claimed by the present invention, Applicants respectfully submit that the present invention is patentably distinct thereover. Reconsideration and withdrawal of the rejections are respectfully requested.

**2. Claim Rejections: 35 USC § 103(a): Claims 1, 5, 6, 8 and 9**

Claims 1, 5, 6, 8 and 9 stand rejected as being obvious over Albert (US 5545396) in view of either DE 29609958 or Walther. This rejection is respectfully traversed.

The Examiner suggests that it would be obvious to combine the teaching of either DE'958 or Walther on silica-coated vials with that of Albert. However, Applicants point out that such a combination is directly contrary to the teaching of Albert.

Albert at Example 2 (Column 19 lines 1 to 55, especially lines 1-14) specifically teaches that a silicone coating is to be used and is effective to reduce relaxation of the hyperpolarised  $^{129}\text{Xe}$  gas on the walls of the glass vessel. Applicants submit that silicone is a "synthetic polymer containing a repeating silicon oxygen backbone with organic side groups attached *via* carbon-silicon bonds (Merck Index, 13<sup>th</sup> Edition, entry no. 8569). The present claims specify silica, re.  $\text{SiO}_2$  which is not carbon-containing.

Applicants respectfully submit that Albert provides a clear teaching that the problem is already solved by a silicone coating. Therefore, a proper reading of Albert would teach away

from combining Albert with either of DE'958 or Walther. The Examiner's combination of references is therefore invalid and should be withdrawn.

**3. Claim Rejections: 35 USC § 103(a): Claims 1, 5, 7-9**

Claims 1, 5 and 7-9 are rejected as obvious over the combination of Ardenkjaer-Larsen (US 6466814) with either Schott DE 29609958 or Walther. This rejection is respectfully traversed.

The Examiner implies that Ardenkjaer-Larsen discloses hyperpolarised compositions in vials. Applicants do not agree with this characterisation – there seems to be no such explicit disclosure of vials in this reference.

Applicants note that Column 16 lines 16-28 of Ardenkjaer-Larsen refers to

“.... Containers which contain a plurality of thin-walled tubes of a thin-walled material such as quartz, glass or plastic”.

Such containers do not correspond to vials. Example 2 of Ardenkjaer-Larsen refers to syringes and Examples 3 and 4 to ampoules. The latter are clearly all glass (i.e. the conventional definition), since the Examples refer to flame-sealing and subsequent cracking open.

As the combination put forward by the Examiner would lead to a different type of container than vials, Applicants respectfully submit that such a combination fails to disclose, teach, or suggest the present invention, where a “vial” is an essential feature. Claim 1 is therefore believed non-obvious over this combination, and applicants contend that this objection should be withdrawn. Since claims 2-9 depend on Claim 1, they are also believed to be non-obvious over this combination. Reconsideration and withdrawal of the rejection is respectfully requested.

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Amdt. Dated September 28, 2004  
Reply to Office action of June 29, 2004

In view of the remarks hereinabove, Applicants respectfully submit that the instant application, including claims 1-9, is in condition for allowance. Favorable action thereon is respectfully requested.

Any questions with respect to the foregoing may be directed to Applicants' undersigned counsel at the telephone number below.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'R. Chisholm', written over a horizontal line.

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